REMARKS

Claims 5-81 are currently pending in the application. Applicant notes, with appreciation, the indication that claims 5-20, 22-29 and 35-37 are considered allowable. Accordingly, claims 21, 30-34, and 38-81 are currently under consideration.

Independent claims 21, 38, 64 and 73 were amended to delete from the Markush group the recitation of citric acid and a citrate. Because of the nature of this amendment, it is respectfully submitted that no new matter issues are raised thereby. Accordingly, entry of the amendment and consideration of the claimed subject matter are respectfully solicited.

ISSUE FEE

As indicated by the Examiner, Applicant has paid the issue fee for this application. Applicant hereby requests that the issue fee be held for the benefit of Applicant until prosecution of this application is completed.

ALLOWED CLAIMS

Claims 5-20, 22-29, and 35-37 were indicated as allowable. The Examiner further indicated that claims 39-46 would be allowable if rewritten in independent form. Applicant notes, however, that claim 39 is already in independent form. The claim is directed to a glucose dehydrogenase composition comprising glucose dehydrogenase and phthalic acid or phthalate. Hence, it is respectfully submitted that the subject matter of independent claim 39 is also allowable over the art of record. Claims 40-46 depend directly or indirectly on independent claim 39 and should also be deemed allowable. It is noted that dependent claims 52 and 53 also depend from independent claim 39 and no rejections of the subject matter contained in claims 52 and 53 have been made. Accordingly, it is respectfully submitted that claims 39-46, 52 and 53

are allowable. Reconsideration and the indication of allowability of these claims are respectfully solicited.

REJECTION UNDER 35 U.S.C. § 112

Claims 30-34, 47-51, 59-63, 68-72 and 77-81 were rejected under 35 U.S.C. § 112 as being indefinite. In particular, it was asserted that the scope of the claims could not be determined because of the use of the expression "a derivative thereof". The rejection is traversed and it is respectfully submitted that one of ordinary skill in the glucose sensor arts would have no difficulty understanding the meets and bounds of these claims.

It is well settled that the disclosure of a patent application embraces not only what is expressly set forth in words, but also what persons skilled in the art would understand. *In re Howarth*, 210 USPQ 689, 692 (Fed. Cir. 1981). It is Applicant's position that those skilled in the relevant art would have no difficulty understanding the scope of the claimed subject matter since the use of the expression "a derivative thereof" describing sugars is precisely the terminology used by those skilled in this art.

In support of the common knowledge of Applicant's terminology in the relevant art, Applicant provides herewith a copy from the page of Scientific Encyclopedia, Eighth Edition, describing the term "derivative". As known in the art, a derivative refers to a compound which is derived from a starting compound through a simple chemical process which maintains the basic structure of the starting material. In further support of the common terminology Applicant is using in this disclosure, Applicant conducted a search of the term "sugar derivative(s)" in the USPTO database. Over four hundred and fifty U.S. Patents contain this term within their specification. A copy of the first few pages of the results of this search is also attached herewith

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for the Examiner's consideration. Hence, it is Applicant's position that since Applicant employs the exact terminology found enabling by several hundred U.S. patents and found in common dictionary references, the expression is understood and the claims will be communicated to the interested public in a meaningful way. Accordingly, reconsideration and withdrawal of the rejection predicated on indefiniteness are respectfully solicited.

Claim 31 was also rejected under 35 U.S.C. § 112, second paragraph, because it apparently was unclear to the Examiner as to how a glucose assay can be stabilized by glucose. Applicant respectfully submits that stabilizing glucose dehydrogenase by glucose is not inconsistent with the claimed subject since the added glucose can be taken into account when measuring the actual sample.

As discussed in the Summary section of the application, an advantage of the present invention is a stable glucose sensor and compositions therefor and a glucose sensor that produces a low blank value. As also discussed in the background of the application, a blank value represents the degree of sensor response when no glucose is present. When glucose is added as a stabilizer, however, a response current value attributed to the stabilizer can be determined and can be ascribe a positive error. Hence, the sum of the blank value and the positive error is the total error in this particular system. Since the amount of stabilizer added to the sensor is known, the positive error is also known. Also since the blank value is determined prior to making the measurement, it is also known. Therefore, the error in the measurement can be corrected prior to taking the measurement of an actual sample.

It should be noted that the problems address by the present invention arise not from the fact that a blank value, or even a positive error, is present, but rather that these values change over time. The presence of a blank value and positive error does not adversely affect the actual

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measurement, however. The reason is that a calibration line, from which the blank value and positive error have been deducted, is formed and the glucose concentration is measured through an electrical treatment based on the calibration line. Hence, it is not inconsistent to use glucose as a stabilizer in the systems. Accordingly, reconsideration and withdrawal of the rejection are respectfully solicited.

REJECTION UNDER 35 U.S.C. § 102

Claims 21, 38, 64 and 73 were rejected as anticipated by JP 409140378 A to Adachi et al. (Adachi) and clams 21, 38, 64, 65, 73 and 74 were rejected as anticipated by U.S. 6,025,203 to Vetter et al. (Vetter). The rejections are traversed and it is respectfully submitted that the claims now in the application are no longer anticipated by the cited references.

The basis for the rejection, according to the Examiner, was that both Adachi and Vetter describe the use of a citrate or citric acid. Applicant has amended independent claims 21, 38, 64 and 73 to exclude therefrom a citrate and citric acid from the Markush group. Hence, it is respectfully submitted that the now claimed subject matter is not anticipated by the cited references. Accordingly, reconsideration and withdrawal of the rejection are respectfully solicited.

REJECTION UNDER 35 U.S.C. § 103

Claims 55, 59-62, 64, 68-73 and 77-81 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. 5,997,817 to Crismore et al. (Crismore) in view of Vetter and U.S. 6,071,391 to Gotoh et al. (Gotoh). The rejection is traversed and it is respectfully submitted that the claims are patentable within the meaning of 35 U.S.C. § 103(a).

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As noted by the Examiner, Crismore does not teach the buffers recited in independent claims 55, 64 and 73. Both Vetter and Gotoh failed to cure this deficiency.

Vetter relates to a diagnostic test carrier that employs a knitted fabric, which allegedly provides the test carrier with certain advantages (See, e.g., col. 2, ll. 48-54). In a particular embodiment, Vetter teaches the use of the knitted fabric in an optical sensor (col. 5, ll. 62-65). Vetter then proceeds to describe a composition for use with the optical sensor, which includes citric acid monohydrate. There is no discussion within Vetter as to the purpose or function of any of the components of the composition. Hence there is no reason why one of ordinary skill in the art would modify the electrochemical biosensor of Crismore with the composition for an optical sensor, as described by Vetter, since Vetter is silent as to the purpose or function of the components of its composition.

It should also be noted that Vetter does not address the problems associated with present invention. For example, the technical significance of the blank value in Vetter is completely different from that of a blank value in an electrochemical glucose sensor. The reason is that in Vetter the blank value is insignificant as long as it employs a substance having low optical (rather than electrical) responsiveness. That is, Vetter teaches the use of substances having low absorption for light at a certain wavelength to maintain a low blank value. Hence, the addition of citric acid in the Vetter glucose sensor is for an entirely different purpose and there is no reason why one of ordinary skill in the art would modify the specific teachings of the primary reference, Crismore, to arrive at the claimed subject matter given the teachings of Vetter.

Gotoh does not cure the deficiencies of Crismore or Vetter. Gotoh teaches a biosensor with a spaced feature therein. This biosensor requires an electrode having an glucose oxidase immobilized thereon (see Abstract). Gotoh teaches that the glucose oxidase can be immobilized

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by forming a layer from glucose oxidase, a 165800-unit component (GOD), and distilled water or a buffered solution (col. 4, ll. 6-24). Gotoh then proceeds to describe several potential compositions containing the GOD component with buffers, such as phosphoric acid (Example A, col. 6, ll. 26-33), citric acid (Example B3, B4, col. 8, ll. 46-56), among others.

Initially, it should be noted, however, that Gotoh has nothing to do with the problems associated with stabilizing a glucose dehydrogenase sensor or compositions thereof. As discussed in Applicant's specification, stability and a low blank value can be achieved by using various additives. These advantages would not be recognized nor appreciated from the teachings of Gotoh.

Although Gotoh discloses that citric acid can be added to a glucose oxidase (GOD, 165800 unit) containing composition to adjust the composition's pH, Gotoh does not recognize the unexpected stability obtained by using citric acid with PQQ-GDH (see Applicant's Example 6, page 20). It should be appreciated that PQQ-GDH and GOD enzymes have different characteristics and responses. PQQ-GDH is an enzyme having a molecular weight of 50 KDa and composed of two subunits, with PQQ serving as the active site. On the other hand, GOD is a longer, spherical enzyme having a molecular weight of 155KDa, with FAD serving as the active site.

An illustration of the different chemical responses of these enzymes is born out by the teachings of Gotoh and the results reported in the present application. For example, Gotoh teaches a sensor employing a phosphoric acid buffer (col. 6, l. 26). Applicant has found, however, that addition of phosphoric acid to PQQ-GDH does not result in a sensor having a good blank value (see, page 4, ll. 13-18 and Comparative Example 1). Hence, while addition of phosphoric acid to PQQ-GDH does not provide good stability against preservation, addition of

phosphoric acid to GOD is known to provide excellent stability (See, Figure 10 of Disposable Biosensor Based on Biochemistry, enclosed herewith). As such, GOD and PQQ-GDH based systems do not behave the same and the results reported in the present application would not have been expected based on the use of a GOD enzyme system. Thus, it is Applicant's position that the teachings of Gotoh would not have realistically motivated one of ordinary skill in the art to modify the other cited references to arrive at Applicant's claimed subject matter. Accordingly, reconsideration and withdrawal of the rejection of claims 55, 59-62, 64, 68-73 and 77-81 are solicited.

Additionally, it should be noted that independent claims 64 and 73 does not include a citrate or citric acid. Hence, even if the Examiner's rationale is correct in that both Vetter and Gotoh stand for the proposition of using a citrate or citric acid as a buffer and that the use of such buffers would be an obvious substitute for the buffer employed in the primary reference, this rationale is no longer applicable with respect to claims 64 and 73. Accordingly, reconsideration and withdrawal of the rejection with respect to independent claims 64 and 73 are additionally solicited.

Based upon the foregoing it is respectfully submitted that the claims now in the application are patentable. Accordingly, reconsideration and allowance of the application are respectfully solicited.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached page is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including

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extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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Marked-up Version Showing Changes Made

Claims 21, 38, 64 and 73 has been amended as follows:

21. (Amended) A method for stabilizing glucose dehydrogenase for use in glucose sensors, wherein at least one additive is added to glucose dehydrogenase whose coenzyme is pyrrolo-quinoline quinone, said additive being selected from the group consisting of phthalic acid, a phthalate, maleic acid, a maleate, triethanol amine, a triethanol amine salt, [citric acid, a citrate,] dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl)aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole or colicin.

38. (Amended) A glucose dehydrogenase composition for use in glucose sensors, said composition containing glucose dehydrogenase whose coenzyme is pyrrolo-quinoline quinone, and at lease one additive selected from the group consisting of phthalic acid, a phthalate, maleic, acid, a maleate, triethanol amine, a triethanol amine salt, [citric acid, a citrate,] dimethyl glutaric acid, (N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl) aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole or colicin.

64. (Amended) A method for stabilizing glucose dehydrogenase for use in glucose sensors, wherein a stabilizer and a buffer are added to glucose dehydrogenase whose coenzyme is pyrrolo-quinoline quinone,

said stabilizer being selected from the group consisting of a metal salt, an organic acid, a protein, and a sugar and a derivative thereof, and said buffer being selected from the group consisting of maleic acid, a maleate, triethanol amine, a triethanol amine salt, [citric acid, a citrate,] dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl) aminomethane, a tris(hydroxymethyl)aminomethane salt, imidazole or colicin.

73. (Amended) A glucose dehydrogenase composition for use in glucose sensors, said composition containing: at least one stabilizer selected from the group consisting of a metal salt, an organic acid, a protein, and a sugar and a derivative thereof; a glucose dehydrogenase whose coenzyme is pyrrolo-quinoline quinone; and a buffer selected from the group consisting of maleic acid, a maleate, triethanol amine, a triethanol amine salt, [citric acid, a citrate,] dimethyl glutaric acid, 2-(N-morpholino)ethane sulfonic acid, a 2-(N-morpholino)ethane sulfonate, tris(hydroxymethyl)glycine, a tris(hydroxymethyl)glycine salt, tris(hydroxymethyl) aminomethane. a tris(hydroxymethyl)aminomethane salt, imidazole or colicin.